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EXAMINER	
LIN, JERRY	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,434	GLINSKII, GUENNADI V.	
	Examiner	Art Unit	
	Jerry Lin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☒ Claim(s) *24-28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6 pages*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-21, in the reply filed on April 4, 2006 is acknowledged. The traversal is on the ground(s) that the claims in Group II (claims 22-28) depend from claim 1 and require all the steps in claim 1. Applicants also amended the claims in Group II to more clearly demonstrate that Group II depends from claim 1. In light of the amendments, the Examiner agrees with the Applicants and will rejoin Group I with Group II (claims 1-28). In addition, applicants also elected Table 5 in response to the species requirement for Group II. Thus the Examiner will examine claims 1-28 and Table 5. Group III (claims 29-32) remain withdrawn as being drawn to an unelected invention.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Claims

Claims 1-28 and Table 5 are under examination.

Claims 29-32 are cancelled (drawn to an unelected invention).

Information Disclosure Statement

2. The PCT search report listed on the Information Disclosure Statement filed April 15, 2005 has not been considered since the search report is not a published document.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. The disclosure contains embedded hyperlinks throughout the specification (for example, pages 68, 72, and 73). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

4. Claims 24-28 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 24 is the most limiting because it requires that every gene in the table be included in the subset. Claims 28 is the least limiting because it only requires that 60% of the genes in the table be included in the subset. However, claim 28 depends from claim 24. Claims 26-27 are also improper under the same analysis.

Claim Rejections - 35 USC § 112, 2nd Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it is unclear what the term "direction" means in line 9. One interpretation of the term is that the common genes have an increased expression in the first sample to second sample and in the third sample to the fourth sample (or decreased expression in the first sample to the second sample and in the third sample to the fourth sample). Another interpretation of the term is that absolute value of differential expression is the same in the first to second sample and the third to fourth sample.

Claim 1 recites the limitation "the direction" in line 9. There is insufficient antecedent basis for this limitation in the claim. This limitation was not recited previously in the claim or in the claim from which it depends.

Claim 22 recites the limitation "the sign" in line 4. There is insufficient antecedent basis for this limitation in the claim. This limitation was not recited previously in the claim or in the claim from which it depends.

Claim 22 is also indefinite because it is unclear what the term "the sign" means. One interpretation is that the second correlation coefficient may be a negative or positive value. Another interpretation is that the second correlation coefficient may include some other variable or value that indicates the positive or negative correlation with a phenotype.

Claims 22-28 are also unclear because the recited tables include genes that are insufficiently described in the specification. Table 5 lists Affymetrix Probe Set ID, LocusLink Identifier, and a Description for each gene. However, the specification does not include any sequence listing that indicates what the gene is. Furthermore, upon

consultation with the Scientific and Technical Information Center, the instant claims are not searchable, since the information associated with the Affymetrix Probe Set ID and LocusLink Identifier are frequently updated and the information changes. Because the information is updated frequently, it is unclear what subject matter is claimed and is to be searched.

Claim Rejections - 35 USC § 112, 1st Paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 24-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Instant claims 24-28 are drawn to identifying the subset of genes in Table 5. In order for one of skill in the art to specifically know what gene is cited in the claims at the time of filing, one of skill in the art requires a gene sequence. However, instant specification has no gene sequence. Instead, Table 5 provides an Affymetrix Probe Set ID, LocusLink Identifier, and a Description that is usually the gene's protein product. However, the information on Table 5 does not describe the genes themselves. Footnote 1 on the page 87 of the instant specification states sequences of the gene

may be obtained from the NCBI website through LocusLink. However, public databases, such as LocusLink, frequently update the sequences and the information found on each sequence is dynamic. Thus citing a public database does not adequately describe the gene the applicants intended to include in their claims at the time of filing. Likewise citing the ID number from a private company also does not adequately describe the gene, since the ID numbers of private companies are also subject to change. Since neither the LocusLink nor the Affymetrix Probe Set ID adequately describe the gene that the claims are intending to encompass at the time of the filing, the applicants must provide a sequence listing of each gene in order for one of skill in the art to know that the inventor had possession of the claimed invention at the time the application was filed. Since the applicants have not provided any gene sequence information, claims 24-28 fail to comply with the written description requirement.

9. Claims 24-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Given that the instant claims do not comply with the written description requirement, one skill in the art would not be able to determine a subset of genes that

consists essentially of the genes in Table 5 because one skill in the art would not know what the genes are in Table 5.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 1-28 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The instant claims are drawn to identifying a subset of genes using a correlation coefficient calculated from gene expression data.

In regards to claims 1-28, the instant claims are drawn to a mathematical algorithm of determining the correlation of gene expression data. A mathematical algorithm is non-statutory unless the claims include a step of physical transformation, or if the claims include a useful, tangible and concrete result. It is important to note, that the claims themselves must include a physical transformation step or a useful, tangible and concrete result in order for the claimed invention to be statutory. It is not sufficient that a physical transformation step or a useful, tangible, and concrete result be asserted in the specification for the claims to be statutory. In the instant claims, there is no step of physical transformation, thus the Examiner must determine if the instant claims include a useful, tangible, and concrete result.

In determining if the instant claims are useful, tangible, and concrete, the Examiner must determine each standard individually. For a claim to be "useful," the

claim must produce a result that is specific, substantial, and credible. For a claim to be "tangible," the claim must set forth a practical application of the invention that produces a real-world result. For a claim to be "concrete," the process must have a result that can be substantially repeatable or the process must substantially produce the same result again. Furthermore, the claim must recite a useful, tangible, and concrete result in the claim itself, and the claim must be limited only to statutory embodiments. Thus, if the claim is broader than the statutory embodiments of the claim, the Examiner must reject the claim as non-statutory.

The instant claims do not include any tangible result. A tangible requirement requires that the claim must set forth a practical application of the mathematical algorithm to produce a real-world result. The instant claims are drawn to identifying a subset of genes using a correlation coefficient calculated from gene expression data such as mRNA quantification data, cRNA quantification data, cDNA quantification data, etc. However, the method as claimed, does include any step of conveying results to the real world. Without such a conveyance, the method does not necessarily have a real-world result. Thus the instant claims do not include any tangible result.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Backert et al. (Int. J. Cancer (1999) Volume 82, pages 868-874) in view of Bertucci et al. (Human Molecular Genetics (2000) Volume 9, Number 20, pages 2981-2991).

The instant claims are drawn to identifying a subset of genes using a correlation coefficient calculated from gene expression data.

Regarding 1, Backert et al. teach using two samples that different with respect to phenotype and determining a reference set of genes (page 869, left column; page 870, paragraph bridging left and right column), identifying a second reference set of expressed genes from a third and fourth sample (page 870, right column, second full paragraph); identifying a concordance set of expressed genes (page 870, right column, bottom full paragraph).

However, Backert et al. do not teach determining a correlation coefficient that exceeds a predetermined value.

Bertucci et al. teaches determining the correlation coefficient that exceed a predetermine value for correlating genes (page 2987, right column, 2nd full paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the methods of Backert et al. with Bertucci et al. to gain the advantage of determining the reproducibility of experiments. One of the challenges that face gene expression experiments is the precision of the equipment used in those experiments. Given the same experiment, the equipment may produce different results. Given the uncertainty of the equipment as well as the need to compare data from different sources, one of ordinary skill in the art would seek to verify the reproducibility

of experiments to ensure that their interpretation of the data is correct. Backert et al. recognized the need to find determine the accuracy of gene expression experiments (page 871, right column, under discussion). Bertucci et al. teaches a method of determining the accuracy of gene expression using a correlation coefficient (page 2987, right column, 2nd full paragraph). Given that Backer et al. recognizes the need for determining the accuracy of a gene expression experiment, and Bertucci et al. provides for such a need, one of ordinary skill in the art would be motivated to combine the methods of Backert et al. and Bertucci et al. to ensure that the gene expression data was accurate.

Regarding claims 2-6, Bertucci et al. teach determining a correlation coefficient (page 2987, right column, 2nd full paragraph); logarithmically transforming the differentials (page 2987, right column, 3rd full paragraph); wherein the correlation coefficient has an absolute value greater than 0.98 (page 2987, right column, 2nd full paragraph).

Regarding claims 8-11, Bertucci et al. teach wherein the gene expression data is cDNA or RNA quantification data (page 870); wherein the sample comprises of a cell line, which is a tumor cell line (page 869, left column, top).

Regarding claims 16-19, Bertucci et al. teach wherein the sample is from a patient, a healthy donor, is a tumor cell, or from the colon (paragraph bridging pages 869-867).

Regarding claim 20, Bertucci et al. teach where the phenotype is selected from lymph node status (page 2983, left column, bottom section).

Regarding claim 21, Bertucci et al. teach where a plurality of independent samples is used for each sample (paragraph bridging page 869-870); and where the differential is an average over the sample (page 870, Table II).

Regarding claim 22, Bertucci et al. teach determining a second correlation coefficient with a positive sign that establishes a positive correlation with a phenotype (page 2983, right column, first full paragraph).

Regarding claim 23, Bertucci et al. teach that ERBB2 had the highest correlation of the genes tested (page 2983, first full paragraph) and since its correlation was the highest its correlation was the most reliable indication of cancer (abstract; page 2985, left column, bottom paragraph – right column, top paragraph).

14. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Backert et al. (Int. J. Cancer (1999) Volume 82, pages 868-874) in view of Bertucci et al. (Human Molecular Genetics (2000) Volume 9, Number 20, pages 2981-2991) further in view of Young et al. (US #2005/0255588 A1).

The instant claims are drawn to identifying a subset of genes using a correlation coefficient calculated from gene expression data and using samples comprising omnipotent or pluripotent cells.

Backert et al. and Bertucci et al. are applied as above.

However, neither Backert et al. nor Bertucci et al. teach using pluripotent or omnipotent stem cells.

Young et al. teach creating samples of pluripotent or omnipotent stem cells (page 3, paragraph 0019-0020).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the cell lines described in Young et al. with the methods of Backert et al. and Bertucci et al. The motivation to combine Backert et al. with Bertucii et al. is provided above. It is recognized in the art the use of stem cells could potentially provide many new applications in science and medicine (Young et al., page 3, paragraph 0015-0016). However, it is unclear genes are expressed to maintain a cell as a stem cell. Thus one of ordinary skill in the art seeking to understand the gene expression of stem cells would be motivated to determine what genes are differentially expressed that correspond to the stem cell phenotype. Backert et al. provide a method of identifying the correct identification of the differences in gene expression between different cell lines (Backert et al., page 873, right column, bottom). Backert et al.'s method could identify the differences in gene expression in a stem cell as compared to other cells. Thus one of ordinary skill in the art seeking to understand the gene expression of stem cells would be motivated to take the sample cell lines disclosed by Young et al. and use those samples in the method provided by Backert et al.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 10:00am-6:30pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Representatives are available to answer your questions daily from 6 am to midnight (EST). When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system

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